

W:\BioTransplant, Inc\08477,989 Certif. of Kieber.doc

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:

Bazin et al.

Serial No:

08/477,989

Filed:

June 7, 1995

Art Unit: 1806

Examiner: Gambel, P.

Title:

LO-CD 2a Antibody and Uses for Inhibiting T-Cell Activation and Proliferation

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

DECLARATION OF THOMAS KIEBER-EMMONS

Thomas Kieber-Emmons declares as follows:

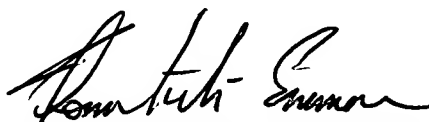
1. He is one of the inventors of the referenced application.
2. He is familiar with U.S. Patent 5,283,058 ("Queen") which is directed to the production of humanized antibodies wherein certain amino acids of the acceptor antibody (human antibody framework) are not retained in the humanized antibody.
3. Queen discloses certain criteria for such substitution, namely, the amino acid is (i) within a certain distance from a CDR (less than 6 angstroms); (ii) is adjacent to a CDR; (iii) interacts with a CDR; or (iv) the amino acid for the acceptor at the position is "rare" and the corresponding amino acid of the donor is "typical." Queen defines the meaning of "rare" and "typical."
4. In the claimed humanized antibody, the amino acids of the humanized antibody in both the light and heavy chain framework which are changed from those present in the human acceptor framework do not meet any of the above criteria disclosed by Queen.
5. In producing the claimed humanized antibody, the change of acceptor framework amino acids in the humanized antibody was based on criteria different than those disclosed by Queen and, therefore, do not meet the above criteria established by Queen; i.e., the changed acceptor (human) framework amino acids of the claimed humanized antibody are not within 6

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angstroms of the CDR; are not adjacent to a CDR; do not interact with a CDR and are not "rare" at the position as defined in the Queen patent.

6. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 6/18/98



THOMAS KIEBER-EMMONS